Published in final edited form as:
Gynecol Oncol. 2012 September ; 126(3): 351–356. doi:10.1016/j.ygyno.2012.05.008.

Rhabdomyosarcoma of the Cervix in Adult Women and Younger Patients

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Abstract

Objectives—Cervical rhabdomyosarcoma is extremely rare, and there is a paucity of literature on the subject. The purpose of this study was to describe the clinical and pathologic features of cervical rhabdomyosarcoma.

Methods—We retrospectively reviewed all patients with cervical rhabdomyosarcoma who presented to our institution from 1980–2010. We reviewed pathologic, demographic, and clinical information.

Results—During the study period, 11 females presented with cervical rhabdomyosarcoma. The median age at presentation was 18.4 years, and 6 patients were <19 years old at diagnosis. Vaginal bleeding was the most common presenting symptom, and a vaginal mass was often a co-presenting symptom. Eight patients (73%) presented with stage IB disease, and 8 (73%) presented with the embryonal (botryoid) histologic subtype. Nine patients (82%) received multimodal therapy consisting of surgery with chemotherapy, radiation therapy, or both. All patients were without evidence of disease after completion of primary therapy, but 3 patients experienced local recurrence. At a median follow-up of 23 months, 6 patients (55%) were without evidence of disease, 1 (9%) was alive with disease, 1 (9%) had died of disease, and 3 (27%) had died of other causes. Three patients (27%) had other primary malignancies in addition to rhabdomyosarcoma—1 had a Sertoli-Leydig tumor, 1 had a Sertoli-Leydig tumor and a pinealoblastoma, and 1 had thyroid cancer and a parotid adenocarcinoma.

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Disclosures: The authors have no conflicts of interest to disclose

Conclusions—With multimodal therapy, cervical rhabdomyosarcoma appears to be associated with a good prognosis. Favorable prognostic factors such as early stage at diagnosis and a favorable histologic subtype may contribute to the excellent observed survival.

Keywords

cervix; rhabdomyosarcoma; Sertoli-Leydig tumor

Introduction

Rhabdomyosarcoma is a malignant neoplasm arising from skeletal muscle progenitors. In children, rhabdomyosarcoma is the most common soft tissue tumor, responsible for approximately 50% of all soft tissue sarcomas and 3% to 4% of all cancers. [1] Rhabdomyosarcomas in children occur most commonly in the head and neck region; the genitourinary tract is the second most common primary tumor location. [2] In adults, rhabdomyosarcomas are rare, accounting for less than 5% of all soft tissue sarcomas and less than 1% of all malignancies. [3] Recently, the Intergroup Rhabdomyosarcoma Study Group reported a new classification of rhabdomyosarcoma in which tumors are divided into 3 major histologic subtypes: embryonal, alveolar, and undifferentiated. The embryonal subtype is the most common, accounting for 58% of all rhabdomyosarcomas. The embryonal subtype is further classified into classic, botryoid, and spindle cell subtypes, which account for 49%, 6%, and 3% of all rhabdomyosarcomas, respectively. [4]

Although approximately 20% of rhabdomyosarcomas in children arise in the genitourinary tract, [5] only 0.5% of primary rhabdomyosarcomas in girls are found on the cervix. [6] Primary cervical rhabdomyosarcoma in adults is even rarer. Ferguson et al [5] found only 8 cases of adult cervical rhabdomyosarcoma diagnosed over 40 years at Memorial Sloan-Kettering Cancer Center. In contrast to its more common vaginal counterpart, which most commonly occurs in the first decade of life, cervical embryonal rhabdomyosarcoma most commonly occurs in the second and third decades of life. [7] There is no standard treatment for patients with rhabdomyosarcoma of the cervix, although most patients are treated with a combination of surgery and chemotherapy.

Because of the extreme rarity of cervical rhabdomyosarcoma, the literature on this disease consists mainly of case reports, [4–6] and no large case series have been published. Furthermore, all of the small case series that do exist focus either on a pediatric or an adult population—no publications consider the disease across all age groups. The purpose of this study was to describe the clinical and pathologic features of cervical rhabdomyosarcoma and to see whether treatment and outcomes differ between adult women and younger females.

Materials and Methods

This study was conducted with approval from the Institutional Review Board at The University of Texas MD Anderson Cancer Center. We reviewed the medical records of all patients who presented to MD Anderson with a diagnosis of cervical rhabdomyosarcoma from January 1, 1980, to December 31, 2010. Clinical and pathologic records were reviewed. Surgical pathology reports were reviewed to obtain data from gross and histopathologic review. Histopathologic diagnoses were then confirmed for this study by gynecologic and/or sarcoma pathologists at MD Anderson. Patients were excluded if the rhabdomyosarcoma component was part of a biphasic tumor or a germ cell tumor, if they were diagnosed as having cervical rhabdomyosarcoma but the pathology report showed the tumor to originate elsewhere (e.g., in the uterus), or if the pathology report was available but

no clinical records were available (e.g., pathology consultation only and patient not seen at MD Anderson).

Demographic and clinical information, including age at time of diagnosis, race/ethnicity, body mass index, presenting symptoms, prior medical history, and tumor characteristics, were obtained from medical records, as was information about treatment and follow-up. Stage was determined according to 2 different systems: the Intergroup Rhabdomyosarcoma Study Group clinical classification system, which groups patients on the basis of extent of disease, resectability, and microscopic evaluation of surgical margins (Table 1), [5] and the TNM staging system for rhabdomyosarcoma (Table 2). [8] On the basis of information in prior publications on rhabdomyosarcoma, the age of 19 years was used as the cut-off in the classification of pediatric versus adult patients. [9]

Results

Between 1980 and 2010, 18 cases of cervical rhabdomyosarcoma were seen at MD Anderson. Seven cases were excluded as only pathology review was performed. Therefore, 11 patients with cervical rhabdomyosarcoma were included in this review. Patient and tumor characteristics are summarized in Table 3. The median age at diagnosis was 18.4 years, and 6 patients (55%) were younger than 19 years at diagnosis. Vaginal bleeding or discharge was present in all 11 patients, and 4 patients (36%) had a vaginal mass as a co-presenting symptom. At presentation, the median tumor size was 4 cm (range, 1–22 cm). Eight patients (73%) had the embryonal (botryoid) variant of cervical rhabdomyosarcoma, while 2 patients (18%) had non-botryoid embryonal tumors. One patient (9%) had undifferentiated cervical rhabdomyosarcoma. On TNM classification, 4 patients (36%) had T1a tumors, 3 patients (27%) had T1b tumors, and 2 patients (18%) had T2a tumors. All patients were without nodal metastases and distant metastases according to findings on physical examination, imaging, and/or surgical resection. Using the FIGO clinical staging system for cervical cancer, 4 patients (36%) had stage IB1 disease, 4 patients (36%) had stage IB2 disease, and 1 patient (9%) had stage IIA disease. Two patients had no staging information available. All 9 patients whose tumor description was available had an exophytic tumor at diagnosis. Nine patients (82%) had disease classified as Intergroup Rhabdomyosarcoma Study Group clinical group I.

Demographic and clinical features by patient are presented in Table 4. Primary treatment was surgery in 9 patients (82%) and chemotherapy in 2 patients (18%). All patients received surgery at some point during treatment. Cone biopsy or polypectomy was performed in 8 patients (73%), and total abdominal hysterectomy was performed in 3 patients (27%). Only 1 patient (patient 2 in Table 4) had a postoperative complication: significant vaginal bleeding after conization necessitating uterine artery embolization.

At the end of primary therapy, all 11 patients had no evidence of disease. At a median follow-up of 23 months (range, 1–176 months), 3 patients (27%) had experienced local recurrence. No patients had distant metastasis at recurrence. At recurrence, 1 patient (patient 3 in Table 4) received 2 cycles of ifosfamide before dying from complications related to neutropenic fever. The other 2 patients declined treatment. At last follow-up, 1 had died of disease, and the other was alive with disease. Of the 8 patients who did not experience recurrence (n=7) or for whom information about recurrence was not available (n=1), 6 (75%) were alive at last follow-up, 1 (9%) had died of parotid adenocarcinoma, and 1 (9%) had died of an unknown cause.

Table 5 compares tumor characteristics, treatments, and outcomes by age (younger than 19 years versus 19 years or older). Histologic type and stage at presentation were similar between patients younger than 19 years and those 19 years of age or older.

Three patients (27%) had been diagnosed with other malignancies before being diagnosed with cervical rhabdomyosarcoma. Two of these patients had previously been diagnosed with pediatric ovarian sex cord stromal tumor, an exceedingly rare disease in its own right. One patient (patient 11 in Table 4) had been diagnosed with a high-grade mixed Sertoli-Leydig and granulosa cell tumor at age 15 years. She underwent fertility-sparing unilateral salpingo-oophorectomy followed by 6 cycles of carboplatin and paclitaxel and was without evidence of disease at completion of therapy. Thirty-two months after completion of chemotherapy, she was noted to have a new exophytic cervical lesion, which was proven by biopsy to be rhabdomyosarcoma. She was treated with cervical conization followed by vincristine, dactinomycin, and cyclophosphamide. At last follow-up, 8 months after completion of chemotherapy, she was without evidence of disease. A second patient (patient 1 in Table 4) was diagnosed at age 10 years with a pinealoblastoma, for which she was treated with radiation therapy followed by cyclophosphamide, vincristine, and cisplatin. At age 16 years, she was diagnosed with a Sertoli-Leydig tumor of the ovary, for which she underwent a unilateral salpingo-oophorectomy. One year later, she was diagnosed with a recurrence of the Sertoli-Leydig tumor as well as a new cervical rhabdomyosarcoma. These tumors were treated with a fertility-sparing unilateral ovarian cystectomy and cervical conization followed by vincristine, dactinomycin, and cyclophosphamide. At last follow-up, 25 months after her last chemotherapy treatment, she was without evidence of disease. A third patient (patient 4 in Table 4) was diagnosed with thyroid cancer at age 22 years. She was treated with a thyroidectomy and was subsequently without evidence of disease. At age 49 years, she was diagnosed with cervical rhabdomyosarcoma. She underwent a hysterectomy and was treated with external-beam and vaginal dome radiotherapy as well as cyclophosphamide, doxorubicin, vincristine, and dacarbazine. She had no evidence of disease after treatment. At 55 years, the patient was diagnosed with an unresectable high-grade adenocarcinoma of the right parotid. The tumor metastasized to the lung, and 6 months after her diagnosis of parotid adenocarcinoma, the patient died from this disease.

Discussion

The prognosis associated with cervical rhabdomyosarcoma appears to be favorable: only 1 of the 11 patients in this series succumbed to her disease. Furthermore, this patient declined treatment at diagnosis of recurrence, so it remains unclear if her disease may have responded to treatment.

Although no definitive conclusions regarding prognosis can be made on the basis of a small study such as this, many favorable prognostic factors for rhabdomyosarcoma at other sites were present in our cohort. For example, in our study, all 9 of the patients for whom a tumor description was available had an exophytic mass on the cervix. While studies on rhabdomyosarcoma of the cervix are mainly limited to case reports, a study of rhabdomyosarcoma in the urinary bladder and vagina by Leuschner et al [10] showed that classical embryonal rhabdomyosarcoma most commonly presented with a polypoid (exophytic) growth pattern and that this growth pattern was associated with a more favorable prognosis (92% 10-year survival rate) than a diffuse intramural (endophytic) growth pattern (68% 10-year survival rate, $P = .02$). A summary of cervical rhabdomyosarcomas studies is shown in Table 6.

In addition, 8 of the patients in our series (73%) had the botryoid variant of embryonal rhabdomyosarcoma. The embryonal botryoid variant is associated with a much more

favorable outcome than the alveolar and undifferentiated subtypes, which are associated with a particularly poor prognosis.[4] Two patients had embryonal rhabdomyosarcoma with the exact variant unknown, and the 1 patient with undifferentiated rhabdomyosarcoma died from a complication of chemotherapy and we cannot determine what her survival would have been otherwise.

Another highly favorable prognostic factor—early disease stage at diagnosis—was present in a large proportion of our patients; no patient in our series had disease spread beyond the cervix or vagina at diagnosis. The early stage at diagnosis was most likely related to early appearance of symptoms. All patients in our series presented with vaginal bleeding or discharge, and many noted a mass protruding from the vagina.

No nodal or distant metastases were noted for any of the patients in our series. In a study by Esnaola et al [11] about the predictors of survival in patients with rhabdomyosarcoma, age, tumor location, nodal status, and histologic subtype did not appear to be associated with survival in adults with rhabdomyosarcoma treated with multimodal therapy. However, metastatic disease at presentation and poor response to chemotherapy were strongly associated with poor prognosis. While that study included 39 patients, none had cervical rhabdomyosarcoma. With so few cases of cervical rhabdomyosarcoma reported in the literature, it is difficult to extrapolate from the findings of ours and other studies to draw broad conclusions about the impact of nodal metastases on survival.

Our study compared disease presentation, treatment, and outcomes between women 19 years of age or older and younger patients. However, because of the small sample sizes, no meaningful statistical analyses could be performed. A study by Sultan et al [9] that included 1,071 adults (age > 19 years) and 1,529 children (age ≤ 19 years) showed that adults with rhabdomyosarcoma (all sites) had a significantly worse outcome than children (5-year overall survival rate, 27% ± 1.4% versus 61% ± 1.4%; $P < 0.0001$). Tumors in adults were more likely to be at an unfavorable site (65% versus 55%; $P < 0.0001$) and to be of histologic subtypes that are unusual during childhood, particularly the pleomorphic subtype (19%) and not otherwise specified (43%). Adults also had significantly worse outcomes than children with similar tumors.[9] Sultan et al noted that the majority of the children in their series presented with embryonal rhabdomyosarcoma. As the majority of the patients in our series (10 of 11) also presented with embryonal rhabdomyosarcoma, one might conclude that age is not as great a predictor of outcome as is the histologic variant. However, the number of cases of cervical rhabdomyosarcoma was not specifically noted in the Sultan et al study as it was a general rhabdomyosarcoma study.

An interesting finding in our study was that 3 of the 11 patients had multiple primary cancers. Two patients presented with Sertoli-Leydig tumors. In a review of the literature, we found 5 reports describing the same situation. McClean et al [7] reported a case of embryonal rhabdomyosarcoma of the cervix and ovarian Sertoli-Leydig cell tumor of intermediate differentiation in a 13-year-old girl. Golbang et al [12] reported a girl who presented with cervical sarcoma botryoides tumor at age 14 years and a right ovarian Sertoli-Leydig cell tumor at 27 years. Daya and Scully [13] reported 2 patients with cervical sarcoma botryoides who had previously undergone oophorectomy for a Sertoli-Leydig tumor. A recently published study of cervical rhabdomyosarcoma by Dehner et al. [14] reported a 13-year old girl with cervical embryonal rhabdomyosarcoma who also had a Sertoli-Leydig cell tumor of the right ovary as well as nodular hyperplasia of the thyroid. All 5 previously reported cases of Sertoli-Leydig cell tumors in association with cervical embryonal rhabdomyosarcoma were of intermediate differentiation [7, 12–14]. One of the patients in our series who had a cervical rhabdomyosarcoma and a Sertoli-Leydig tumor also had a prior history of a pinealoblastoma. While we found 2 reports of a pineal teratoma

giving rise to a rhabdomyosarcoma, [15] we found no reports showing a link between cervical rhabdomyosarcoma and pinealoblastoma. The third patient in our series who had multiple primary tumors had a history of thyroid cancer (type unknown) and parotid adenocarcinoma. We were unable to find any studies that showed a link between these multiple primary tumors. However, rhabdomyosarcoma in general has already been associated with certain inherited diseases, including Li-Fraumeni syndrome, neurofibromatosis type 1, Beckwith-Wiedemann syndrome, Costello syndrome, Noonan syndrome, and MEN2A syndrome. A case report by Mousavi and Akhavan [16] also described the presence of cervical sarcoma botryoides in 2 sisters, highlighting the possible role of genetic factors in the development of sarcoma botryoides. Dehner et al. [14] found a *DICER 1* germline mutation in a 9 year old girl with cervical rhabdomyosarcoma and pleuropulmonary blastoma pointing to possible genetic predisposition to developing these malignancies. Others have also associated mutations in *DICER1* with familial pleuropulmonary blastoma syndrome. Schultz et al. [17]reported on three children with pleuroplumonary blastoma and Sertoli-Leydig tumors of the ovary. Furthermore, another three family members of patients with pleuropulmonary blastoma also had Sertoli Leydig tumors. The discovery of a *DICER1* mutation in this familial syndrome is of particular interest as 60% of Sertoli-Leydig tumors have this mutation [18].

Another interesting observation in our study was that with the exception of the 2.9-year-old patient, only 2 patients had a body mass index within the normal limits of 18.5–24.9 kg/m^2. Three patients were in the overweight category, and 5 patients were in the obese category, 3 of whom had a body mass index of over 35 kg/m^2. High birth weight and larger than expected size at birth have been linked with an increased risk of embryonal rhabdomyosarcoma. [19] Considering that high birth weight is also associated with a higher body mass index later on in life, [20] it may be of interest to study whether increased body mass index is correlated with increased risk of rhabdomyosarcoma.

The wide variety of regimens received by these patients is attributable to not only the long study period but also the wide range of ages in the patients treated. Over the last decade, however, our multidisciplinary approach has effectively narrowed our management of these patients. In particular, our pediatric patients are co-managed by both gynecologic oncologists and pediatric medical oncologists and typically now undergo local resection (cone biopsy or polypectomy) followed by vincristine, actinomycin-D, and cyclophosphamide (VAC). This regimen is based on 4 studies by the Intergroup Rhabdomyosarcoma Study Group (ISRG) [6]. Those studies moved from aggressive surgery (hysterectomy) and radiation to intensive primary chemotherapy (VAC) with no appreciable change in survival (5 year survival 82% for surgery/radiation vs. 84% for chemotherapy) while maintaining fertility and reducing long-term morbidity from radiation therapy. In addition to VAC chemotherapy, we currently perform a cone biopsy or polypectomy to establish a definitive diagnosis, reduce tumor burden, and minimize symptomatology of vaginal discomfort, bleeding and discharge. We have largely reserved radiation for salvage therapy in the recurrent setting or for patients of advanced age who might not tolerate intensive chemotherapy.

Overall, the findings from our small series indicate that the embryonal subtype of cervical rhabdomyosarcoma is the most frequent subtype and that cervical rhabdomyosarcoma often presents at an early stage (stage I was most common in our series) with vaginal bleeding. Surgery and chemotherapy are the mainstays of treatment of cervical rhabdomyosarcoma, and the prognosis of patients treated with multimodal therapy is very good. We found no differences in treatment or survival between women 19 years or older and younger patients. There may be a genetic link between cervical rhabdomyosarcoma and other primary tumors, most notably Sertoli-Leydig tumor.

Acknowledgments

This research was supported in part by the National Institutes of Health through MD Anderson's Cancer Center Support Grant, CA016672.

References

1. Ries, LAGHD.; Krapcho, M.; Mariotto, A.; Miller, BA.; Feuer, EJ.; Clegg, L.; Eisner, MP.; Horner, MJ.; Howlader, N.; Hayat, M.; Hankey, BF.; Edwards, BK., editors. SEER Cancer Statistics Review, 1975–2003. Bethesda: National Cancer Institute; 2006.
2. Baiocchi G, Faloppa CC, de Toledo Osorio CA, Kumagai LY, Fukazawa EM, Cunha IW. Embryonal rhabdomyosarcoma of the uterine cervix in a 47-year-old woman. J Obstet Gynaecol Res. 2011; 37:940–946. [PubMed: 21410833]
3. Adams BN, Brandt JS, Loukeris K, Holcomb K. Embryonal rhabdomyosarcoma of the cervix and appendiceal carcinoid tumor. Obstet Gynecol. 2011; 117:482–484. [PubMed: 21252797]
4. Ghaemmaghami F, Karimi Zarchi M, Ghasemi M. Lower genital tract rhabdomyosarcoma: case series and literature review. Arch Gynecol Obstet. 2008; 278:65–69. [PubMed: 18427824]
5. Ferguson SE, Gerald W, Barakat RR, Chi DS, Soslow RA. Clinicopathologic features of rhabdomyosarcoma of gynecologic origin in adults. Am J Surg Pathol. 2007; 31:382–389. [PubMed: 17325479]
6. Arndt CA, Donaldson SS, Anderson JR, Andrassy RJ, Laurie F, Link MP, Raney RB, Maurer HM, Crist WM. What constitutes optimal therapy for patients with rhabdomyosarcoma of the female genital tract? Cancer. 2001; 91:2454–2468. [PubMed: 11413538]
7. McClean GE, Kurian S, Walter N, Kekre A, McCluggage WG. Cervical embryonal rhabdomyosarcoma and ovarian Sertoli-Leydig cell tumour: a more than coincidental association of two rare neoplasms? J Clin Pathol. 2007; 60:326–328. [PubMed: 17347287]
8. Lawrence W Jr. Gehan EA, Hays DM, Beltangady M, Maurer HM. Prognostic significance of staging factors of the UICC staging system in childhood rhabdomyosarcoma: a report from the Intergroup Rhabdomyosarcoma Study (IRS-II). J Clin Oncol. 1987; 5:46–54. [PubMed: 3543238]
9. Sultan I, Qaddoumi I, Yaser S, Rodriguez-Galindo C, Ferrari A. Comparing adult and pediatric rhabdomyosarcoma in the Surveillance, Epidemiology and End Results program, 1973 to 2005: an analysis of 2,600 patients. J Clin Oncol. 2009; 27:3391–3397. [PubMed: 19398574]
10. Leuschner I, Harms D, Mattke A, Koscielniak E, Treuner J. Rhabdomyosarcoma of the urinary bladder and vagina: a clinicopathologic study with emphasis on recurrent disease: a report from the Kiel Pediatric Tumor Registry and the German CWS Study. Am J Surg Pathol. 2001; 25:856–864. [PubMed: 11420456]
11. Esnaola NF, Rubin BP, Baldini EH, Vasudevan N, Demetri GD, Fletcher CD, Singer S. Response to chemotherapy and predictors of survival in adult rhabdomyosarcoma. Ann Surg. 2001; 234:215–223. [PubMed: 11505068]
12. Golbang P, Khan A, Scurry J, MacIsaac I, Planner R. Cervical sarcoma botryoides and ovarian Sertoli-Leydig cell tumor. Gynecol Oncol. 1997; 67:102–106. [PubMed: 9345364]
13. Daya DA, Scully RE. Sarcoma botryoides of the uterine cervix in young women: a clinicopathological study of 13 cases. Gynecol Oncol. 1988; 29:290–304. [PubMed: 3278956]
14. Dehner LP, Jarzembowski JA, Hill DA. Embryonal rhabdomyosarcoma of the uterine cervix: a report of 14 cases and a discussion of its unusual clinicopathological associations. Mod Pathol. 2012; 25:602–614. [PubMed: 22157934]
15. Preissig SH, Smith MT, Huntington HW. Rhabdomyosarcoma arising in a pineal teratoma. Cancer. 1979; 44:281–284. [PubMed: 455253]
16. Mousavi A, Akhavan S. Sarcoma botryoides (embryonal rhabdomyosarcoma) of the uterine cervix in sisters. J Gynecol Oncol. 2010; 21:273–275. [PubMed: 21278891]
17. Schultz KA, Pacheco MC, Yang J, Williams GM, Messinger Y, Hill DA, Dehner LP, Priest JR. Ovarian sex cord-stromal tumors, pleuropulmonary blastoma and DICER1 mutations: a report from the International Pleuropulmonary Blastoma Registry. Gynecol Oncol. 2011; 122:246–250. [PubMed: 21501861]

18. Heravi-Moussavi A, Anglesio MS, Cheng SW, Senz J, Yang W, Prentice L, Fejes AP, Chow C, Tone A, Kalloger SE, Hamel N, Roth A, Ha G, Wan AN, Maines-Bandiera S, Salamanca C, Pasini B, Clarke BA, Lee AF, Lee CH, Zhao C, Young RH, Aparicio SA, Sorensen PH, Woo MM, Boyd N, Jones SJ, Hirst M, Marra MA, Gilks B, Shah SP, Foulkes WD, Morin GB, Huntsman DG. Recurrent somatic DICER1 mutations in nonepithelial ovarian cancers. N Engl J Med. 2012; 366:234–242. [PubMed: 22187960]

19. Ognjanovic S, Carozza SE, Chow EJ, Fox EE, Horel S, McLaughlin CC, Mueller BA, Puumala S, Reynolds P, Von Behren J, Spector L. Birth characteristics and the risk of childhood rhabdomyosarcoma based on histological subtype. Br J Cancer. 2010; 102:227–231. [PubMed: 19997102]

20. Curhan GC, Willett WC, Rimm EB, Spiegelman D, Ascherio AL, Stampfer MJ. Birth weight and adult hypertension, diabetes mellitus, and obesity in US men. Circulation. 1996; 94:3246–3250. [PubMed: 8989136]

Highlights

- Cervical rhabdomyosarcoma appears to have a good prognosis
- Multimodal therapy often successfully controls disease
- As many patients are young, fertility sparing therapies should be considered

TABLE 1

Intergroup Rhabdomyosarcoma Study Group Clinical Classification System for Rhabdomyosarcoma [8]

Clinical Group	Extent of Disease, Resectability, and Margin Status
I	A: localized tumor, confined to site of origin, completely resected
	B: localized tumor, infiltrating beyond site of origin, completely resected
II	A: localized tumor, gross total resection, but with microscopic residual disease
	B: locally extensive tumor (spread to regional lymph nodes), completely resected
III	A: localized or locally extensive tumor, gross residual disease after biopsy only
	B: localized or locally extensive tumor, gross residual disease after major resection (≥ 50% debulking)
IV	Any size primary tumor, with or without regional lymph node involvement, with distant metastases, irrespective of surgical approach to primary tumor

TABLE 2

TNM Staging System for Rhabdomyosarcoma [8]

Stage	Sites	T	Tumor Size Designation	N	M
I	Orbit	T1 or T2	a or b	Any N	M0
	Head and neck*				
	Genitourinary†				
	Biliary tract				
II	Bladder or prostate	T1 or T2	a	N0 or Nx	M0
	Extremity				
	Cranial parameningeal				
	Other‡				
III	Bladder or prostate	T1 or T2	a	N1	M0
	Extremity				
	Cranial parameningeal				
	Other‡				
IV	All	T1 or T2	a or b	N0 or N1	M1

T1, tumor confined to anatomic site; T2, tumor extension; a, ≤ 5 cm in diameter; b, > 5 cm in diameter; N0, nodes not clinically involved; N1, nodes clinically involved; Nx, clinical status of nodes unknown; M0, no distant metastases; M1, distant metastases present.

*Excluding parameningeal sites.

†Nonbladder and nonprostate.

‡Includes trunk, retroperitoneum, etc., excluding biliary tract.

TABLE 3

Patient and Tumor Characteristics

Characteristic	No. of Patients (%)
Median age (range)	18.4 years (2.9–51.9 years)
Median body mass index (range)	28.9 kg/m^2 (20.4–78.1 kg/m^2)*
Race/ethnicity	
Caucasian	8 (73%)
African American	2 (18%)
Hispanic	1 (9%)
Presenting symptom	
Vaginal bleeding	10 (91%)
Vaginal mass	4 (36%)
Vaginal discharge	1 (9%)
Other primary malignancy	
None	8 (73%)
Sertoli-Leydig tumor	2† (18%)
Pinealoblastoma	1† (9%)
Thyroid cancer (unknown type)	1‡ (9%)
Adenocarcinoma of parotid	1‡ (9%)
Clinical stage	
IB1	4 (36%)
IB2	4 (36%)
IIA	1 (9%)
Unknown	2 (18%)
Median tumor size	4 cm (range, 1–22 cm)
IRSG classification	
Group 1	9 (82%)
Unknown	2 (18%)
Histological variant	
Embryonal (botryoid variant)	8 (73%)
Embryonal (non-botryoid)	2 (18%)
Undifferentiated	1 (9%)

IRSG, Intergroup Rhabdomyosarcoma Study Group.

*A 2.9-year-old patient in whom body mass index could not be accurately assessed was not included.

†One patient had both Sertoli-Leydig tumor and pinealoblastoma.

‡One patient had both thyroid cancer and parotid adenocarcinoma.

TABLE 4

Demographic and Clinical Features by Patient

No.	Age, years	Tumor Site	Stage	Primary Treatment	Adjuvant Treatment	Treatment for Recurrence	Status at Last Follow-up
1	17.8	Cervix	IB1	Cone biopsy	Vincristine, dactinomycin, and cyclophosphamide	NA	NED 23 mo after completion of therapy
2	12.5	Cervix	IB2	Cone biopsy	Vincristine, dactinomycin, and cyclophosphamide	NA	NED 6 mo after completion of therapy
3	33.3	Cervix	IB1	TAH and BSO	Cisplatin and doxorubicin. Treated immediately after surgery with whole-pelvic and intracavitary vaginal radiation to 45 Gy	Chemotherapy	Dead of complications related to neutropenic fever
4	49.3	Cervix and lower uterine segment	IB1	TAH and BSO	Cyclophosphamide, doxorubicin, vincristine, and dacarbazine. Radiation beginning 6 mo after diagnosis: 46 Gy delivered over 31 days	NA	Dead of parotid adenocarcinoma
5	51.9	Cervix	IB2	Cone biopsy	NA	NA	NED 19 mo after completion of therapy
6	2.9	Cervix and midposterior vagina	IIA	Polypectomy	Vincristine, dactinomycin, and cyclophosphamide	NA	NED 35 mo after completion of therapy
7	12.7	Endocervix extending to vagina	IB2	VAC	TAH	NA	NED 121 mo after completion of therapy
8	17.3	Cervix	NA	Cone biopsy	Vincristine, doxorubicin, and cyclophosphamide	Refused chemotherapy	Dead of disease
9	34.2	Cervix	NA	VAC, FAC	Cone biopsy	Not known whether patient had recurrence	Dead of unknown cause

No.	Age, years	Tumor Site	Stage	Primary Treatment	Adjuvant Treatment	Treatment for Recurrence	Status at Last Follow-up
10	27.2	Cervix	IB2	Cone biopsy	NA	Refused chemotherapy	Alive with disease
11	18.4	Cervix	IB1	Cone biopsy, diagnostic laparoscopy	Vincristine, dactinomycin, and cyclophosphamide	NA	NED 4 mo after completion of therapy

NA, Not applicable – patient did not have recurrence; NED, no evidence of disease; TAH; total abdominal hysterectomy; BSO, bilateral salpingo-oophorectomy; VAC, vincristine, dactinomycin, and cyclophosphamide; FAC, fluorouracil, doxorubicin, and cyclophosphamide.

TABLE 5

Comparison of patients < 19 years old and ≥ 19 years old

	Patients < 19 Years (n=6)	**Women ≥ 19 Years (n=5)**
Histology	Embryonal (Botryoid variant) (5)	Embryonal (Botryoid variant) (3)
	Embryonal, variant unknown (1)	Embryonal, variant unknown (1)
		Undifferentiated (1)
Tumor stage	IB1 (2)	IB1 (2)
	IB2 (2)	IB2 (2)
	IIA (1)	Unknown (1)
	Unknown (1)	
Primary treatment	Cone biopsy (4)	Cone biopsy (2)
	Polypectomy (1)	TAH and BSO (2)
	Chemotherapy (1)	Chemotherapy (1)
Adjuvant treatment	Chemotherapy (5)	Chemoradiation (2)
	TAH (1)	None (2)
		Cone biopsy (1)
Status at last follow-up	No evidence of disease (4)	Dead of other cause (2)
	Alive with disease (1)	No evidence of disease (1)
	Dead of disease (1)*	Alive with disease (1)
		Unknown (1)

TAH, total abdominal hysterectomy; BSO, bilateral salpingo-oophorectomy.

*Patient was < 19 years of age at diagnosis. Patient had a recurrence at >19 years of age.

TABLE 6

Overview of Previously Published Studies of Cervical Rhabdomyosarcoma

First Author	Year	No. of Pts.	Tumor Information**	Proportion of Pts. < 19 Years	Recurrence Rate
Daya [13]	1988	13	Embryonal (Botryoid variant); presented with vaginal bleeding (9/13) or protruding mass (4/13); surgery (13/13) and chemotherapy (5/13)	62% (8/13)	0% (1 died of disease)
Golbang [12]	1997	1	Embryonal (Botryoid variant); presented with vaginal bleeding and protruding mass; stage 1B; surgery	100%	0%
Bernal [19]	2004	1	Embryonal (Botryoid variant); presented with vaginal bleeding and protruding mass; surgery and chemotherapy	100%	100%
McClean [7]	2007	1	Embryonal (unknown variant); presented with amenorrhea; polypectomy	100%	Unknown
Koukourakis [20]	2009	1	Embryonal(unknown variant); presented with vaginal bleeding; surgery, chemotherapy, and radiotherapy	0%	0%
Mousavi [16]	2010	2	Embryonal (Botryoid variant); presented with vaginal bleeding and protruding mass; stage IA; surgery	100%	Unknown (1 died of disease, other with no evidence of disease)
Cakar [21]	2011	1	Alveolar; presented with vaginal bleeding and protruding mass; surgery and chemotherapy	100%	100% (died of disease)
Smrkolj [22]	2011	1	Embryonal(unknown variant); presented with vaginal bleeding; surgery, chemotherapy, and radiotherapy	100%	0%
Adams [3]	2011	1	Embryonal (unknown variant); presented with menorrhagia; surgery and chemotherapy	0%	Unknown
Ocheke [23]	2011	1	Embryonal (unknown variant); presented with vaginal bleeding and protruding mass; stage II; surgery	100%	100% (died of disease)
Baiocchi [2]	2011	11	Embryonal (Botryoid variant); presented with protruding mass; stage IA[†]; surgery (11/11), radiotherapy (4/11), and chemotherapy (6/11)	0%	45% (5/11)[‡]
Dehner [14]	2011	14	Embryonal (unknown variant); presented with vaginal bleeding and cervical polyp; surgery (13/14) and chemotherapy (13/14)	85% (12/14)	14% (2/14)

Pts., patients.

*Variant of cervical rhabdomyosarcoma, presenting symptoms, stage, and treatment. If information is not provided, it was unavailable.

†Tumor information available for only 1 patient; the other patients were reviewed in other articles.

‡Four of these patients did not receive adjuvant chemotherapy and died from disease.